

### Remarks

Applicants appreciate the Examiner's allowance of claims 6-15, and have amended Claim 1 herewith. Claims 2-15 are unchanged.

Rejection of claims 1 and 3-4 under 35 U.S.C. 102(b) as anticipated by Zanakis et al.

The Examiner has rejected claims 1 and 3-4 under 35 U.S.C. 102(b) as anticipated by U.S. Patent No. 5,433,735 to Zanakis et al. ("Zanakis" hereafter). The Examiner contends Zanakis shows a method of increasing angiogenesis in a muscle tissue by applying an electrical voltage to the tissue wherein the voltage does not cause contraction of the muscle.

Applicants have amended claim 1 such that the method of the present invention is directed to a method for inducing angiogenesis in a muscle tissue wherein angiogenesis comprises an increase in capillary density. Zanakis does not disclose an increase in capillary density by application of electric voltage such that there is no muscle contraction. In contrast to Zanakis, the instant application discloses and claims inducing angiogenesis comprising an increase in capillary density without inducing muscle contraction. For example, on page 13, lines 20-34, angiogenesis is shown by an increase in capillary density. Further, in Figure 7, capillary density of electrostimulated ischemic rat muscles is shown to have been increased by about 2.5-fold as compared with the contralateral (non-ischemic) muscles while unstimulated and sham-operated animals had no significant difference in capillary density. Further, representative images of the stimulated and unstimulated muscle are shown in Figure 8, again demonstrating an increase in capillary density according to the method of the present invention.

Accordingly, because the disclosure of Zanakis does not disclose increasing capillary density in a muscle tissue by applying electrical voltage, Applicants respectfully assert that Zanakis does not anticipate amended claim 1 and its dependent claims 3 and 4.

Rejection of claim 2 under 35 U.S.C. 103(a) as unpatentable over Zanakis et al.

The Examiner contends that Zanakis discloses the claimed invention except for the electrical voltage being 0.1V at 50Hz. However, as discussed above, claim 1 has been amended

such that the method of the present invention is directed to inducing angiogenesis in a muscle tissue wherein angiogenesis comprises an increase in capillary density. Accordingly, because the disclosure of Zanakis does not in any way teach, suggest or motivate increasing capillary density, Applicants respectfully assert that Zanakis does not render claim 2 obvious, as claim 2 is dependent on amended claim 1.

Rejection of claim 4 under 35 U.S.C. 103(a) as unpatentable over Zanakis et al.

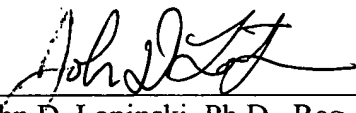
The Examiner contends that Zanakis fails to specifically point out that muscle cells are cardiac muscle cells, but Zanakis teaches that it is an object of the invention disclosed therein to promote blood infusion in damaged tissues, and it would have been an obvious design choice to include cardiac muscle cells in the method of Zanakis because cardiac muscle cells are subject to ischemia. However, as described above, Applicants have amended claim 1 such that the method of the present invention is directed to a method for inducing angiogenesis in a muscle tissue wherein angiogenesis comprises inducing an increase in capillary density. Accordingly, because the disclosure of Zanakis does not in any way teach, suggest or motivate increasing capillary density, Applicants respectfully assert that Zanakis does not render claim 4 obvious, as claim 4 is dependent on amended claim 1.

**Conclusion**

Based on the above arguments and amendments, Applicants believe that claims 1-15 are in condition for allowance and therefore respectfully request the Examiner to allow all the claims.

It is believed that no additional fee is due with this communication. If any additional fee is due it may be charged to deposit account number 08-2442.

Respectfully submitted,  
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